

## REMARKS/ARGUMENTS

Basis for the amendment to claim 1 involving the support may be found in original claims 12 and 13. Basis for the amendment to claim 1 involving affixing in gelatin may be found in original claims 13 and 14. Basis for the new claims 19 and 20 may be found in original claims 12, 14 and 20.

In paragraph 2 of the Office Action, claims 1-7, 10-12, and 14-18 stand ejected under 35 U.S.C. 103(a) as being unpatentable over Zyomyx, Inc. in view of Marks et al. The Examiner states that:

“Zyomyx discloses protein arrays comprising a substrate, an organic thin film, and proteins immobilized on the thin film (p. 5 lines 6-12). The substrates may be coated before the addition of the organic thin film (p. 19 lines 20-29), where the organic thin film is preferably a monolayer having the formula X-R-Y which fits the applicant's trifunctional compound (p. 22 lines 8-20). The linking group R preferably comprises an alkyl chain having from 8-22 carbons, suggesting through-bond paths connecting the functional groups of not greater than 10 atoms (p. 25 line 27-p. 26 line 5). The functional group X interacts with the substrate or coated substrate by chemical or physical means, where X includes isothiocyanate and isocyanate groups (p. 26 lines 14-22). Functional group Y interacts with a protein by covalent or non-covalent linkage, where Y includes aldehydes, maleimides, iodoacetyl, hydrazide, epoxy, aziridine, vinylsulfone, isothiocyanate, and isocyanates groups (p. 28 line 9-p. 29 line 9). Additionally, an affinity tag attached to the Y functional group include glutathione S-transferase or streptavidin groups (p. 33 lines 19-21). Antibodies, known protein capture agents, are noted as proteins to be immobilized on the thin film (p. 33 lines 1-11). A plurality of proteins are attached to different patches on the substrate (p. 5 lines 1-25). However, the reference does not point to gelatin as a coating substance for the substrates. Marks teaches protein assays using coated substrates, teaching the conventionality of coating gelatin on substrates to reduce non-specific binding (col. 32 line 59-col. 33 line 5; col. 33 lines 39-43). Such coatings also simplify covalent conjugation and enhance signal detection. Because Zyomyx is also concerned with non-specific binding (p. 12 lines 17-19), it is the examiner's position that it would have been prima facie obvious to include a gelatin on

Zyomyx's substrate to reduce non-specific binding, simplify covalent conjugation, and enhance signal detection.

Regarding the coating coverage of gelatin on the substrate, it is the examiners position that it would have been prima facie obvious to coat any amount necessary to optimize the non-specific binding, covalent conjugation, and signal detection properties of the coating."

This rejection is respectfully traversed.

WO 00/04382 A1 (Zyomyx) discloses protein arrays that are fundamentally different from our invention in both array structure and array composition. The Zyomyx WO 00/04382 arrays consist of a substrate on which a thin film is coated, and a plurality of patches on known regions of the thin film. The protein conjugation reagents having formula X-R-Y are located on the surface of each patch with monolayer coverage, generally referred to as organic thinfilm. This structure has been describe in WO 00/04382 on page 15 lines 8-27; page 16 lines 1-12, under "Arrays of proteins" as well as in Figs. 1 to 7. The organic thinfilm in WO 00/04382 A1 has been described as less than 20 nm thick, and gelatin is not disclosed in WO 00/04382 A1 as a material of choice for forming either the coating or the organic thinfilm. It also should be noted that in WO 00/04382 A1 the coating and the organic thinfilm are spatially separated layers with the protein conjugation reagents X-R-Y located in organic thinfilm. In contrast, our invention consists of a substrate on which a layer gelatin is coated, and the protein conjugation reagents having formula X-R-Y are uniformly distributed. Our invention does not consist of any patches on the surface, and our invention of combining X-FR-Y with gelatin as an integral entity greatly simplifies the process of making protein arrays. The difference between our invention and WO 00/04382 is further clarified in the Attachment 1 with this amendment. The binding feature in our invention has been intrinsically incorporated into the surface that only requires one additional step of surface treatment with a buffer solution containing any amino acids.

Mark et al. U.S. 5,977,322 col. 32 line 59-col. 22 line 5; col. 33 lines 39-43, the entire invention discloses a class of novel antibodies and teaches how to use such antibodies in an immunoassay. It is well known that, in performing an immunoassay, the surface, after immobiization of antibodies, is

treated with a solution of protein e.g. BSA, or gelatin, to reduce non-specific binding (see "Elisa: Theory and Practice" (Methods in Molecular Biology, Vol. 42) by John R. Crowther, 1995). However, U.S. 5,977,322 teaches neither how to use gelatin to prepare a protein array nor how to incorporate protein conjugation reagents -R-Y into a gelatin coating to immobilize a protein. In fact, U.S. 5,977,322 has nothing to do with the field of protein arrays but simply mentions about using gelatin to block non-specific binding in a standard immunoassay process and does not suggest combination with WO 00/04382.

There is no disclosure suggestion in any combination of Mark et al. and WO 00/04382 that would lead one to the instant invention where a continuous gelatin is treated with the protein conjugation reagents to result in the substrate as instantly claimed. Therefore, it is respectfully requested that this rejection be reconsidered and withdrawn.

Claims 8-9 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Zyomyx, Inc. (WO 00/04382 A1) in view of Marks et al. (U.S. Patent No. 5,977,322) as applied to claims 1-7, 10-12 and 14-18 above, and further in view of *Kirk-Othmer Encyclopedia of Chemical Technology*.

Zyomyx and Marks apply as above, failing to mention the type of gelatin used in the coating. The *Kirk-Othmer Encyclopedia of Chemical Technology* teaches first that type B gelatin, produced by alkaline processing, has a more reproducible isionic point (section 3.3). The isoionic point is important in reducing viscosity (section 3.4), which eases processing. It is the Examiner's position that it would have been prima facie obvious to use type B gelatin, being alkaline pretreated, because of its reduced viscosity to ease the processing of coatings in the invention of Zyomyx and Marks.

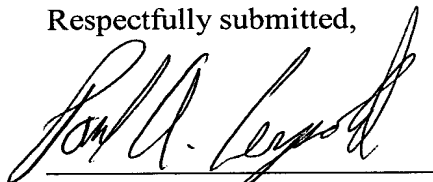
Also, *Kirk-Othmer Encyclopedia of Chemical Technology* notes pork skin as a conventional source for both types A and B gelatin (section 4), where pork skins yield large amounts of gelatin. It is the Examiner's position that it would have been prima facie obvious to choose pig gelatin in the invention of Zyomyx and Marks, since pig gelatin is readily available. Motivation for choosing pig gelatin would have been to maximize the amount of gelatin obtained from the source. This rejection is respectfully traversed.

As was urged above, there is no suggestion in WO 00/04382 Zyomyx to treat a continuous gelatin base with protein conjugation reagent to form a substrate as instantly claimed. The further combination with Kirk-Othmer does not make obvious to modification of Zyomyx to the claimed invention. Therefore, it is respectfully requested that this rejection be reconsidered and withdrawn.

The applicant gratefully notes that in paragraph 8 of the Office Action claim 13 is objected to is being dependent upon a rejected base claim but would be allowable if rewritten in independent form including all the limitations of the base claim and intervening claims. Amended claimed 12 is claim 13 written in independent form, and therefore should be allowable. While the applicant is grateful for the notice of an allowable claim; for the reasons above it is respectfully urged that this invention is deserving of greater protection as set forth in the other claims.

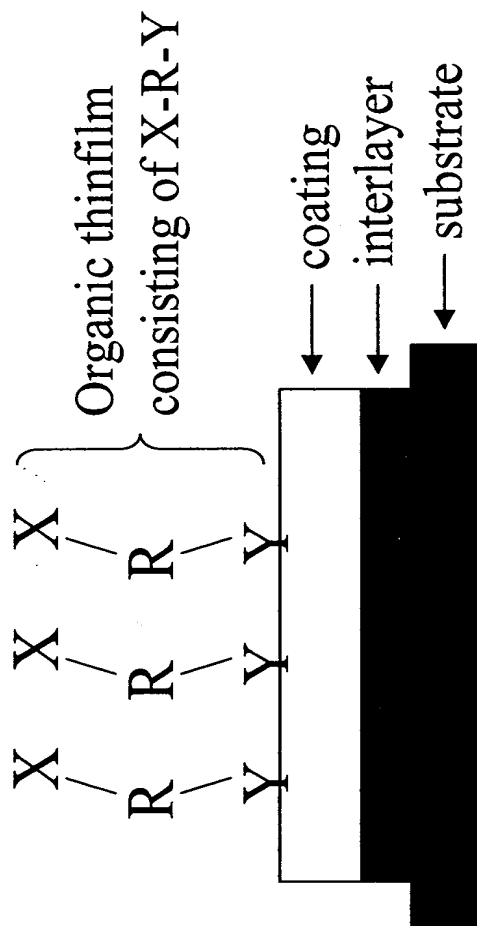
Therefore, it is respectfully requested that the rejection under 35 USC 103 be reconsidered and withdrawn and that an early Notice of Allowability be issued in this application.

Respectfully submitted,

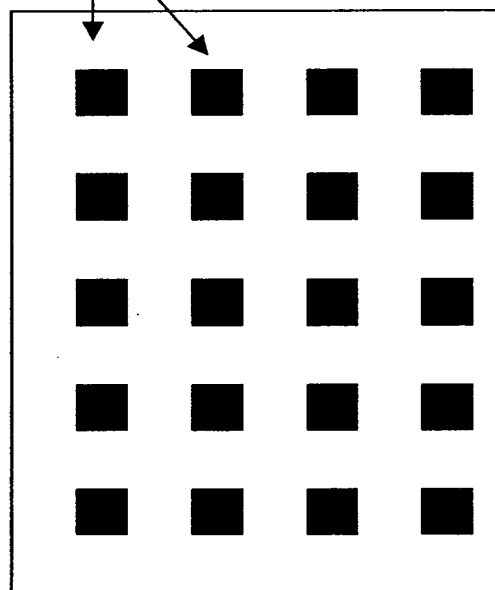
A handwritten signature in dark ink, appearing to read "Paul A. Leipold", written over a horizontal line.

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Registration No. 26,664

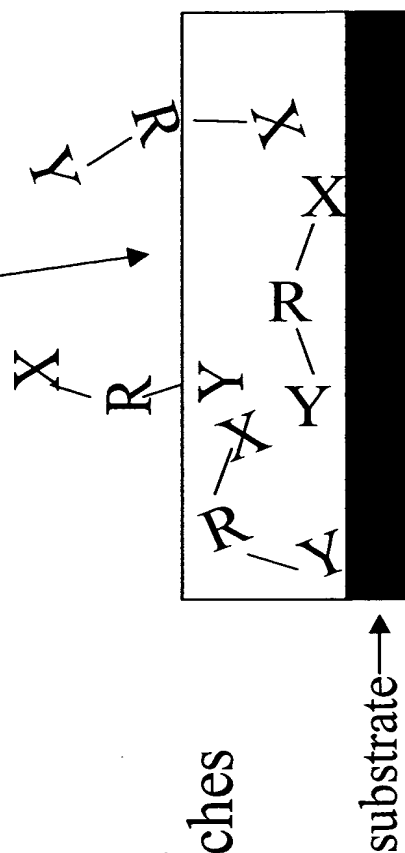
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Single patch



Gelatin coating layer  
consisting of X-R-Y



substrate

The invention